REMARKS

Claims 1, 3, 5-10, and 16-17 have been amended. Claims 19 and 20 were cancelled with the Examiner's Amendment of Paper No. 8. New claims 21-25 are added. Claims 1-18 and 21-25 are now pending in this application. Support for the amendments is found in the existing claims and the specification as discussed below. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Allowable subject matter

Applicants gratefully acknowledge the Examiner's indication of allowable subject matter for claims 6, 10, and 12. Claims 6, 10, and 12 have been rewritten in independent form as claims 22, 23, and 24, respectively. These claims, at least, are believed to be patentable over the art of record.

Personal Interview

Applicants' representative would like to thank Examiner Jennifer Kolb Michener for the courtesy of a Personal Interview on June 25, 2003 with Dan Altman and Che Chereskin. During the interview, agreement was reached with regards to amendments to place the claims in condition for allowance. The amendments discussed included limitation of the claims to medical devices, limiting the frequency of the hydrogen peroxide gas plasma, and/or clarifying the order of the method steps. In view of that interview, the present Amendment is believed to place the application in condition for allowance.

Rejection under 35 U.S.C. § 102(a)

Claims 1-5, 7, 11, and 13-18 are rejected under 35 U.S.C. § 102(a) as being anticipated by Gesche, et al. (DE 199 44 631 A1).

The Examiner asserts that Gesche, et al. teach a method of using microwave plasma to simultaneously coat and sterilize a material. An English translation of the Gesche, et al. patent DE 199 44 631A1 is submitted herewith as Attachment A.

It is respectfully submitted that Gesche et al. does not anticipate the claims as amended. In order to have anticipation, all of the claim elements must be found within the cited document. Gesche et al. do not teach all of the elements of Applicants' invention as presently claimed.

The present claims 1 and 16 have been amended to specify that the material which is coated with the bioactive coating, polymerized and sterilized is a medical device. Support for

this amendment is found on page 8, lines 11-12 of the present specification. In contrast, the teaching of Gesche, et al. is drawn to coating and sterilizing bottles and the apparatus taught by Gesche, et al. is adapted for hollow bodies, that is, bottles (see page 3, last paragraph of Gesche, et al. translation).

The presently claimed invention is further distinguished from Gesche et al. in that Gesche et al. teach that the energy for the ignition and the operation of the plasma is 2.45 GHz or higher. In contrast, Applicants teach an energy of 0.1 MHz to about 30 MHz. This teaching is found in claim 12 of U.S. Patent No. 5,656,238 which was incorporated into the present application specifically by reference at page 9, line 11 of the present specification. New claim 21 is added with the limitation that the frequency energy is 0.1 MHz to 30 MHz. Gesche, et al. teach away from this frequency by teaching that a much higher frequency is required for sterilization and coating.

Applicants also add new claim 25. Claim 25 specifies that the material with the polymerized chemical is sterilized along with a biological indicator. While the material is coated, the biological indicator is not. Support for this claim is found in Example 5 of the present specification. Clearly, the teaching of Gesche, et al. does not meet all of the limitations of claim 25 because in the teaching of Gesche, et al. everything within the sterilization chamber is coated and sterilized. Consequently, it would not be possible to have a item which had been treated with a polymerized bioactive coating sterilized along with a biological indicator which did not have the coating.

Claims 22-24 recite the limitations of claims 6, 10, and 12 and have been indicated as allowable as discussed above.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of the above ground of rejection for all claims is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 8-9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gesche, et al.

The Examiner asserts that while Gesche, et al teach that the method of their invention may be used to coat plastic bottles, Gesche et al. do not specifically teach the bottle materials of claims 8 and 9. However, it is the Examiner's position that it is well known in the bottling

industry to use PET beverage bottles with a fluoroelastomer, that PET is a type of polyethylene and that the fluoroelastomer meets the limitation of claim 9.

In response, PET is not a type of polyethylene. PET is a condensation copolymer of terephthalic acid and ethylene glycol with different properties from polyethylene, an addition polymer of ethylene. Consequently, Applicants assert that the polyethylene of claim 8 is not obvious in view of PET.

Although Applicants do recite poly (ethylene terephthalate) in claim 15, Applicants assert that all of the claims are patentable over Gesche et al. for the reasons given below.

The present claims 1 and 16 have been amended to specify that the material which is coated with the bioactive coating, polymerized and sterilized is a medical device. Support for this amendment is found on page 8, lines 11-12 of the present specification. The medical devices of Applicants' invention include a range of diverse sizes and shapes such as catheters, tissue engineering scaffolds, drug delivery carrier materials, stents to reduce clotting and restenosis, and dental or ophthamological implants. Applicants' claimed method is able to accommodate a diverse range of materials because the method is not restricted to a particularly adapted apparatus as in Gesche, et al. In contrast, the teaching of Gesche, et al. is drawn to coating and sterilizing bottles and the apparatus taught by Gesche, et al. is adapted for hollow bodies, that is, bottles (see page 3, last paragraph & page 5, paragraph 2 of Gesche, et al. English translation). Gesche, et al. do not provide motivation to coat and sterilize medical devices because the disclosure of Gesche, et al. is drawn to hollow tubes and teaches specifically that "the space between the receiver and the bottle wall should be kept as small as possible" (Gesche, et al., English translation, page 4, line 1) and that inserts for the interior of the bottles provide for homogenousness of the microwave field (page 4, paragraph 4). Thus , the teaching of Gesche, et al. does not teach or suggest geometries other than hollow tubes.

The teaching of Gesche, et al. is directed to the coating of plastic bottles to prevent gas and/or liquid from seeping out of the plastic bottles. One of ordinary skill in the art would not be motivated to practice the method of Gesche et al. with medical devices because medical devices are more varied in size, shape and thickness and the apparatus of Gesche, et al is not adapted for medical devices of diverse size and shape (see the figure in Gesche, et al.).

Furthermore, the practice of the claimed method has the advantage that the Sterrad® system is commercially available for the hydrogen peroxide gas plasma process and can be used

in the claimed method without further modification. There is no need for a specialized apparatus such as taught by Gesche, et al.

The presently claimed invention is further distinguished from Gesche et al. in that Gesche et al. teach that the energy for the ignition and the operation of the plasma is 2.45 GHz or higher. In contrast, Applicants teach an energy of 0.1 MHz to about 30 MHz. This teaching is found in claim 12 of U.S. Patent No. 5,656,238 which was incorporated into the present application specifically by reference at page 9, line 11 of the present specification. New claim 21 is added with the limitation that the frequency energy is 0.1 MHz to 30 MHz. Gesche, et al. teach away from this frequency by teaching that a much higher frequency is required for sterilization and coating.

Applicants also add new claim 25. Claim 25 specifies that the material with the polymerized chemical is sterilized along with a biological indicator. While the material is coated, the biological indicator is not. Support for this claim is found in Example 5 of the present specification. Clearly, the teaching of Gesche, et al. does not meet all of the limitations of claim 25 because in the teaching of Gesche, et al. everything within the sterilization chamber is coated and sterilized. Consequently, it would not be possible to have a item which had been treated with a polymerized bioactive coating sterilized along with a biological indicator which did not have the coating. Gesche, et al. does not teach or suggest sterilization of a biological indicator which had not been treated with a coating along with the coated material.

Claims 22-24 recite the limitations of claims 6, 10, and 12 and have been indicated as allowable as discussed above.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 24, 2003

By: Che S. Chereskin

Che Swyden Chereskin, Ph.D.
Registration No. 41,466
Agent of Record
Customer No. 20,995
(949) 760-0404

H:\DOCS\CSC\JOHNA61\AMD_06_03.DOC
061703

ATTACHMENT A

[19] FEDERAL REPUBLIC OF GERMANY

GERMAN PATENT AND TRADEMARK OFFICE

[12] **Published Patent Application**

[10] **DE 199 44 631 A 1**

[51] Int. Cl.^{7}:
A 61 L 2/08
A 61 L 2/14
A 61 L 2/12
A 61 L 2/52
// A61L 101:12

[21] File no.: 199 44 631.8
[22] Application date: 9/17/1999
[43] Publication date: 3/22/2001

[71] Applicant:
Aurion Anlagentechhnik GmbH, 63500 Seligenstadt, DE

[72] Inventor(s):
Gesche, Roland, Dr., 63500 Seligenstadt, DE; Kessler, Lutz, 61137 Schöneck, DE; Imberger, Tobias, 65510 Idstein, DE; Kovacs, Reinhold, Dr., 63069 Offenbach, DE; Schachler, Edgar, 64859 Eppertshausen, DE; Tobies, Harald, 61130 Nidderau, DE; Wette, Frank, 64287 Darmstadt, DE

[56] Printed documents to be taken into consideration in evaluating patentability:

DE 198 14 865 A1
DE 196 40 528 A1

The following information is taken from the papers submitted by the applicant.

[54] Sterilization and coating of hollow bodies using microwave plasma

[57] Microwave plasmas are suitable for effective destruction of microorganisms in various environments. Typical applications are the extension of the shelf life of foods and pharmaceutical and cosmetic products.

According to the invention, an apparatus and a method are described with which hollow bodies can be both sterilized and coated. The coating is applied to the interior surface of the hollow body and acts as a diffusion barrier for gases, flavorings, and aromas. Both processes can take place simultaneously.

Advantages of microwave plasmas compared with other methods are high concentrations of reactive particles (radicals), ultraviolet radiation, and high-frequency electromagnet fields which in their totality bring about the sterilization. The microwave plasma in addition heats the hollow body material only slightly. Thus it is suitable, for example, for use on thermolabile materials, for example polymer materials, and replaces less gentle methods, for example in filling beverages into plastic bottles.

Description

Object of the application, areas of application

The object of the application is an apparatus in which hollow bodies can be sterilized and their surface can be modified and the methods for so doing.

Microorganisms can be effectively destroyed with microwave plasmas and surfaces can be functionalized. Typical applications are the extension of shelf life of food stuffs and pharmaceutical and cosmetic products.

Microwave plasmas are characterized by especially high concentrations of reactive particles, ultraviolet radiation, particle bombardment, and high frequency electromagnetic fields. Acting together, these properties bring about the sterilization.

The reactive particles are radicals, uncharged intermediate reaction products, ions, and other metastable highly excited species.

The purpose of the surface modification is a barrier in order to avoid or reduce material transport through the hollow body material or out of it into the contents. For this purpose, the interior surfaces of hollow bodies are treated plasma-chemically. What can be involved here is morphological changes of the surface or coatings or both.

Compared with other methods, the microwave plasma leads to an only incidental heating of the hollow body material. Thus it can replace less gentle methods for treatment of thermolabile materials such as plastics. Plastics increasingly are being used as packaging material for liquid food products. Here plasma treatment lends itself to packaging for the purpose of sterilization and reduction of diffusion.

Of special value is the combination of sterilization and surface modification since this new combination method saves at least one processing step which reduces the costs and energy expended up to the present.

It is also advantageous that the use of aggressive chemicals can be avoided since the reactive components are formed only during the plasma treatment and quickly disappear again through disintegration, recombination, and relaxation.

State of the art

Conventional methods for sterilization of beverage containers are based on the use of hot steam or hydrogen peroxide (H_2O_2). The latter can be viewed as the standard method for sterilization of plastic beverage bottles.

In the H_2O_2 technology, the packaging material is wetted with H_2O_2 through immersion baths or through spraying. Activation is effected through heating. The germ-killing effect is based on the oxidizing potential of the H_2O_2.

In steam technology, as a rule the finished packaging by way of example is subjected to saturated steam in a pressure chamber. The effect is based on the influence of moist heat. Plastic packaging easily becomes brittle with this treatment.

There are sterilization methods that are based on high frequency plasmas. Compared with high frequency plasmas, microwave plasmas have the advantages that their plasma density (concentration of charged particles) is greater at the same generator output. Thus a higher density of reactive particles such as radicals is also associated with it which play a significant role in sterilization with plasmas.

The permeation behavior and the migration properties of the polymer packaging materials often are unsatisfactory. They all possess a more or less strongly pronounced permeability for oxygen which can penetrate from outside to within and oxidize the contents as well as for carbon dioxide and aromas which escape to the outside.

With respect to minimization of this material transport through and out of the packaging material, multiple layer preforms (the preliminary stage of the blown plastic bottle) are sometimes produced with intermediate barrier layers in injection molding. A drawback of this method is the high manufacturing costs of such multiple layer preforms.

A combination of sterilization and coating up to now has not been described in the literature.

Description of the apparatus

According to the invention, this set of problems is solved with the apparatus described here. Fig. 1 shows the cross section of the apparatus as a schematic diagram. Its primary components are:

- receiver (1)
- microwave generator (6)
- vacuum pump stand (9)
- pressure measurement (11)
- process gas supply (13)
- computer (14)
- valves (V1, V2)

The receiver (1) functions as a microwave resonator. It is composed of two halves (1.a and 1.b). Both halves are connected through a flange (4). The vacuum-tight connection is made through a sealing O-ring (2) composed of an inert plastic.

According to the invention, the various sizes of the hollow bodies (bottles 2) are taken into consideration through the use of inserts (10) that are modeled approximately in bottle form. The same applies to bottles of differing geometry. Thus the uniformity of the plasma treatment is ensured even for various bottle shapes and sizes.

The space between the receiver and the bottle wall should be kept as small as possible, first in order to maintain a homogenous distribution of power density and second, a small total volume is desirable in order to keep the evacuation times as low as possible.

A central supply through a coaxial antenna (5) serves both the admission of process gases as well as coupling of microwaves (15) that are needed for the generation of plasma. The energy for the ignition and the operation of the plasma is fed from a microwave generator (6). Preferably 2.45 GHz or higher frequencies are used.

Evacuation of the vessel takes place laterally in the vicinity of the neck of the bottle so that as effective a conductance as possible is achieved. For this purpose one or several drilled holes (7) are necessary. To ensure the homogeneousness of the microwave field, the drilled holes must be provided with grating or perforated sheeting (8).

Alternatively, the inserts for various bottle geometries can be formed from perforated sheeting (10) that does not transmit any electromagnetic radiation of this frequency. This construction variant improves the conductance upon evacuation and thus reduces pump-out time.

For process control, a pressure measurement tube (11) is flanged to the side of the receiver (1). Optical monitoring (16) can take place through a window (12) at the bottom of the receiver half (1.b).

Valve V1, which forms the connection to vacuum pump stand (9), is a fast-opening gate. The vacuum pump stand is dimensioned in accordance with the required pump-out times. With a combination of slide vane rotary pump (65 m^3/h) and Roots pump (500 m^3/h), pump-out times of around two seconds can be realized if the suction flange diameter is at least 60 mm.

The process gas supply (13) comprises gas flanges with the necessary components, shut-off devices, and mass flow controllers that regulate the gas flow. In addition to gases, liquids also are possible as reactive components for the plasma. For this purpose, devices for dosing liquids are necessary. The liquids are vaporized within the process gas module and are mixed with the gases. Valve V2 separates the outlets of the process gas supply from the receiver.

All measurement and control lines run to a central computer (14) which assumes process regulation. Connected to it are microwave generator (6), vacuum pump stand (9), pressure measurement tubes (11), process gas supply (13), optical detector (14), and valves (V1, V2).

Description of the Method

Methods will be described with which any desired molded hollow bodies composed of any desired material can be sterilized and surface treated on the interior side.

According to the invention, this method is physically and chemically more gentle and more energy saving than that described under the state of the art since the thermal load is low and process steps are eliminated. Thus this is an innovation that offers technological and economic advantages.

The hollow body, which preferably is a plastic bottle, is placed in the lower portion of receiver (1.b), which is sealed vacuum tight to the top portion (1.a) through a gasket (2). After it has been evacuated to a pressure of 0.01 to 10 mbar, the desired process gas mixture is admitted from the process gas supply (13) and the gas discharge is ignited.

According to the invention, during the plasma treatment either a certain pressure or a certain gas composition can be maintained as a result of which surface layers with a homogenous composition arise. Or the partial pressures of the components [sic], change in accordance with a preselected gradient program, in that the individual mass flows are varied.

The latter makes possible the precipitation of gradient layers the composition of which changes depending on the distance from the surface. Such layers combine two properties optimized to the respective problem. In the present case, an optimal layer adhesion to the side of the hollow body and a good diffusion barrier on the other side are thus obtained.

When the pre-set process time is reached, [the receiver] is flooded with sterile air, the treated hollow body is removed and is immediately sealed free of microbes.

Process gases can be oxygen, nitrogen, hydrogen, noble gases, hydrocarbons, fluorocarbon, water, hydrogen peroxide, and organic silicon compounds.

From the standpoint of process technology, five basic types of plasmachemical surface modifications can be distinguished: fluorination, polymer grafting, silicon oxide coating, polymer coating, and diamond-like carbon (DLC) coating.

In the case of fluorination, only the top most layer of the base material is modified plasma-chemically in that fluorine atoms are embedded. Thus a hydrophobization of the surface is achieved. Higher concentrations of fluorocarbons which are used along with noble gases for this purpose lead to the precipitation of Teflon-like layers (plasma polymerization).

A high degree of cross linking of the polymer surface, which is accompanied by a reduction of permeability, is achieved through polymer grafting. In this case, primarily mixtures of hydrocarbons, noble gases, and hydrogen would be used as plasma gas.

If silicon organyls (*Siliziumorganyle*) are utilized in varying quantity relationships with oxygen and noble gases, the nature of the precipitation can be controlled through management of the process from silicon-like to ceramic, quartz-glass-like.

With hydrocarbons in mixtures with hydrogen, oxygen, and noble gases, polymer layers are obtained with the most varied of properties which are influenced through management of the process.

Under certain conditions that are rich in hydrogen and take place in specific temperature windows, diamond-like layers are also obtained with hydrocarbons.

Patent claims

1. Arrangement for the treatment of substrates in a vacuum receiver characterized in that the substrates are hollow bodies.
2. Arrangement according to claim 1 characterized in that a plasma is ignited for treating the substrates.
3. Arrangement according to claim 2 characterized in that the energy source is radiation in the microwave range.
4. Arrangement according to claim 1 characterized in that the hollow bodies are bottles (3).
5. Arrangement according to claim 4 characterized in that the bottles are constructed of polymer materials.
6. Arrangement according to claim 4 characterized in that the bottles are of glass.
7. Arrangement according to claim 4 characterized in that the bottles serve as containers for food products.
8. Arrangement according to claim 4 characterized in that the bottles are used as containers for cosmetic products.
9. Arrangement according to claim 4 characterized in that the bottles are used as containers for pharmaceutical products.
10. Arrangement according to claim 3 characterized in that the microwave radiation is supplied through a coaxial antenna (5).
11. Arrangement according to claim 1 characterized in that inserts (10) are situated in the receiver.
12. Arrangement according to claim 11 characterized in that the inserts (10) are modeled after the various shapes of hollow bodies (3).
13. Arrangement according to claim 11 characterized in that the inserts are produced from perforated sheeting.
14. Arrangement according to claim 1 characterized in that the receiver has a window (12) for optical process control.
15. Method according to claim 1 characterized in that the treatment serves to sterilize the interior substrate surface.
16. Method according to claim 1 characterized in that the treatment serves for plasmachemical surface modification of the interior substrate surface.
17. Method according to claims 15 and 16 characterized in that both processes, sterilizing and surface modification, are combined in one apparatus.
18. Method according to claim 16 characterized in that the surface modification serves to reduce the transport of material into and out of the bottle wall.
19. Method according to claim 18 characterized in that the surface modification takes place through plasma polymerization.

20. Method according to claim 18 characterized in that the surface modification takes place through plasma fluorination.
21. Method according to claim 18 characterized in that the surface modification takes place through plasma graft polymerization.
22. Method according to claim 8 [sic] characterized in that the surface modification takes place through precipitation of silicon-containing layers.
23. Method according to claim 8 [sic] characterized in that the surface modification takes place through precipitation of diamond-like coats (DLC).
24. Method according to claims 15 and 16 characterized in that oxygen is used as plasma gas.
25. Method according to claims 15 and 16 characterized in that hydrogen is used as plasma gas.
26. Method according to claims 15 and 16 characterized in that hydrogen peroxide is used as plasma gas.
27. Method according to claims 15 and 16 characterized in that nitrogen is used as plasma gas.
28. Method according to claims 15 and 16 characterized in that water is used as plasma gas.
29. Method according to claims 15 and 16 characterized in that fluorocarbons are used as plasma gas.
30. Method according to claim 29 characterized in that the fluorocarbons are tetrafluoromethane.
31. Method according to claims 15 and 16 characterized in that silicon organyls are used as plasma gas.
32. Method according to claim 31 characterized in that the silicon organyls are hexamethyldisiloxane (HMDSO).
33. Method according to claim 31 characterized in that noble gases are used as plasma gas.
34. Method according to claim 33 characterized in that the noble gases are helium.
35. Method according to claim 33 characterized in that the noble gases are argon.
36. Method according to claims 24-35 characterized in that mixtures of the aforementioned gases are used.
37. Method according to claim 36 characterized in that the composition is changed over the processing time.

Accompanied by 1 page(s) of drawings.

– Blank page –

DRAWINGS, PAGE 1

Number: **DE 199 44 631 A1**
Int. Cl.[7]: **A1 61 L 2/08**
Date of publication: March 22, 2001

Sterilization and Coating of Hollow Bodies through Microwave Plasma

Figures

[see source for diagram]

Fig. 1: Schematic drawing of the apparatus for plasma treatment of interior surfaces of hollow bottles